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        (c) 1997 Intl.Translations Ctr.Delft
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See Help News 295
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        (c) 1997 Inst for Sci Info
  File 467:ExtraMED(tm)  1996/Dec
        (c) 1996 Informania Ltd.

      Set  Items  Description
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? s macrophage?

      S1  392932  MACROPHAGE?
? s s1 and rejection

          392932  S1
          118893  REJECTION
      S2    4801  S1 AND REJECTION
? s allograft or xenograft

           61395  ALLOGRAFT
           12752  XENOGRAFT
      S3   72861  ALLOGRAFT OR XENOGRAFT
? s s3 and s2

           72861  S3
            4801  S2
      S4    2415  S3 AND S2
? s s4 and human

Processed  10 of  16 files ...
Processing
Completed processing all files
            2415  S4
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       14715687  HUMAN
     S5    1010  S4 AND HUMAN
? s s5 and dichloromethylene(w)diphosphonate

            1010  S5
            1668  DICHLOROMETHYLENE
            8765  DIPHOSPHONATE
             989  DICHLOROMETHYLENE(W)DIPHOSPHONATE
     S6        0  S5 AND DICHLOROMETHYLENE(W)DIPHOSPHONATE
? s dichloromethylene(w)diphosphonate

            1668  DICHLOROMETHYLENE
            8765  DIPHOSPHONATE
     S7      989  DICHLOROMETHYLENE(W)DIPHOSPHONATE
? s s7 and s5

             989  S7
            1010  S5
     S8        0  S7 AND S5
? s s7 and macrophage

             989  S7
          228532  MACROPHAGE
     S9     334  S7 AND MACROPHAGE
? s s9 and (transplant? or implant? or graft?)

Processed  10 of  16 files ...
Processing
Completed processing all files
             334  S9
          670647  TRANSPLANT?
          387014  IMPLANT?
          365173  GRAFT?
    S10       33  S9 AND (TRANSPLANT? OR IMPLANT? OR GRAFT?)
? rd s10

...completed examining records
    S11       14  RD S10 (unique items)
? t s11/6/1-14


 11/6/1     (Item 1 from file: 5)
13659347     BIOSIS Number: 99659347
  Facilitated engraftment of human hematopoietic cells in severe combined
immunodeficient mice following a single injection of Cl-2MDP liposomes
  Print Number: Biological Abstracts Vol. 104 Iss. 005 Ref. 067746


 11/6/2     (Item 2 from file: 5)
13518961     BIOSIS Number: 99518961
  The role of monocytes and macrophages in delayed xenograft rejection
  Print Number: Biological Abstracts Vol. 103 Iss. 011 Ref. 157799


 11/6/3     (Item 3 from file: 5)
13225067     BIOSIS Number: 99225067
  Influence of macrophage depletion on bacterial translocation and
rejection in small bowel transplantation
  Print Number: Biological Abstracts Vol. 102 Iss. 010 Ref. 140697
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11/6/4 (Item 4 from file: 5)
13103482 BIOSIS Number: 99103482
Failure to reject an allografted tumor after elimination of macrophages in mice
Print Number: Biological Abstracts Vol. 102 Iss. 005 Ref. 068931

11/6/5 (Item 5 from file: 5)
11760346 BIOSIS Number: 98360346
Circulation of Human Hematopoietic Cells in Severe Combined Immunodeficient Mice After Cl-2MDP-Liposome-Mediated **Macrophage** Depletion
Print Number: Biological Abstracts Vol. 100 Iss. 004 Ref. 052184

11/6/6 (Item 6 from file: 5)
11270191 BIOSIS Number: 97470191
Prevention of corneal allograft rejection in rats treated with subconjunctival injections of liposomes containing **dichloromethylene diphosphonate**
Print Number: Biological Abstracts Vol. 098 Iss. 009 Ref. 124503

11/6/7 (Item 7 from file: 5)
10074560 BIOSIS Number: 95074560
THE ROLE OF NATURAL ANTIBODIES AND ABO H BLOOD GROUPS IN **TRANSPLANTATION** OF HUMAN LYMPHOID CELLS INTO MICE

11/6/8 (Item 8 from file: 5)
9056263 BIOSIS Number: 93041263
IS EARLY REPOPULATION OF **MACROPHAGE**-DEPLETED LYMPH NODE INDEPENDENT OF BLOOD MONOCYTE IMMIGRATION?

11/6/9 (Item 1 from file: 144)
13097501 PASCAL No.: 97-0394489
Facilitated engraftment of human hematopoietic cells in severe combined immunodeficient mice following a single injection of Cl SUB 2 MDP liposomes

11/6/10 (Item 2 from file: 144)
12208947 PASCAL No.: 95-0426561
Circulation of human hematopoietic cells in severe combined immunodeficient mice after Cl SUB 2 MDP-liposome-mediated **macrophage** depletion

11/6/11 (Item 1 from file: 155)
08297965 95317538
Role of Kupffer cells in cold ischemia/reperfusion injury of rat liver.

11/6/12 (Item 1 from file: 434)
15668540 Genuine Article#: WY032 Number of References: 65
Title: Transient suppression of **macrophage** functions by liposome-encapsulated drugs (ABSTRACT AVAILABLE)

11/6/13 (Item 2 from file: 434)
15491029 Genuine Article#: WL183 Number of References: 35
Title: Chronic stimulation of the hypothalamus-pituitary-adrenal axis in rats by interleukin 1 beta: Central and peripheral mechanisms (ABSTRACT AVAILABLE)

11/6/14 (Item 3 from file: 434)
13617161 Genuine Article#: QB852 Number of References: 25
Title: RESPONSE OF ALVEOLAR **MACROPHAGE**-DEPLETED RATS TO HYPEROXIA (Abstract Available)
? t s11/7/1-14

11/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

13659347 BIOSIS Number: 99659347
Facilitated engraftment of human hematopoietic cells in severe combined immunodeficient mice following a single injection of Cl-2MDP liposomes
Terpstra W; Leenen P J M; Van Den Bos C; Prins A; Loenen W A M; Verstegen M M A; Van Wyngaardt S; Van Rooijen N; Wognum A W; Wagemaker G; Wielenga J J; Lowenberg B
Dep. Hematol., Univ. Hematol., Univ. Hosp. Dijkzigt, Dr Molewaterplein 40, 3015 GD Rotterdam, Netherlands
Leukemia (Basingstoke) 11 (7). 1997. 1049-1054.
Full Journal Title: Leukemia (Basingstoke)
ISSN: 0887-6924
Language: ENGLISH
Print Number: Biological Abstracts Vol. 104 Iss. 005 Ref. 067746
Transplantation of normal and malignant human hematopoietic cells into severe combined immunodeficient (SCID) mice allows for evaluation of long-term growth abilities of these cells and provides a preclinical model for therapeutic interventions. However, large numbers of cells are required for successful engraftment in preirradiated mice due to residual **graft** resistance, that may be mediated by cells from the mononuclear phagocytic system. Intravenous (i.v.) injection of liposomes containing **dichloromethylene diphosphonate** (Cl-2MDP) may eliminate mouse macrophages in spleen and liver. In this study outgrowth of acute myeloid leukemia (AML) cells and umbilical cord blood (UCB) cells in SCID mice conditioned with a single i.v. injection of Cl-2MDP liposomes in addition to sublethal total body irradiation (TBI) was compared to outgrowth of these cells in SCID mice that had received TBI alone. A two- to 10-fold increase in outgrowth of AML cells was observed in four cases of AML. Administration of 10-7 UCB cells reproducibly engrafted SCID mice that had been conditioned with Cl-2MDP liposomes and TBI, whereas human cells were not detected in mice conditioned with TBI alone. As few as 2 times 10-4 purified CD34+ UCB cells engrafted in all mice treated with Cl-2MDP liposomes. In SCID mice treated with **macrophage** depletion unexpected **graft** failures were not observed. Histological examination of the spleen showed that TBI and Cl-2MDP liposomes i.v. resulted in a transient elimination of all **macrophage** subsets in the spleen, whereas TBI had a minor effect. Cl-2MDP liposomes were easy to use and their application was not associated with appreciable side-effects. Cl-2MDP liposome pretreatment in combination with TBI allows for reproducible outgrowth of high numbers of human hematopoietic cells in SCID mice.

11/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

13518961 BIOSIS Number: 99518961
The role of monocytes and macrophages in delayed xenograft rejection
Fryer J P; Chen S; Johnson E; Simone P; Sun L H; Goswitz J J; Matas A J
Dep. Surg., Northwestrn Univ., 303 E. Superior St., Chicago, IL 60611, USA
Xenotransplantation 4 (1). 1997. 40-48.
Full Journal Title: Xenotransplantation
ISSN: 0908-665X
Language: ENGLISH
Print Number: Biological Abstracts Vol. 103 Iss. 011 Ref. 157799
Despite the development of successful strategies for averting hyperacute rejection (HAR) in both small and large animal xenograft models, a delayed xenograft rejection (DXR) ultimately occurs. This process is characterized by endothelial cell activation and **graft** infiltration with activated monocytes and natural killer (NK) cells. We evaluated the role of monocytes and macrophages in a guinea pig-to-rat model of DXR. Our results suggest that specific interactions between these cells and the xenograft occur that result in their activation, since adoptive transfer of xenoactivated splenocytes significantly accelerated both DXR and allograft rejection, while adoptive transfer of alloactivated splenocytes did not. Furthermore, while normal splenocytes caused antibody-dependent cell-mediated cytotoxicity (ADCC) of xenogeneic endothelial cells, xenoactivated splenocytes caused significantly greater endothelial cytotoxicity by antibody-independent mechanisms. Both normal and xenoactivated splenocytes were significantly less cytotoxic if adherent cells, consisting predominantly of monocytes and macrophages, were first removed. In vivo recipient **macrophage** depletion, using liposome-encapsulated **dichloromethylene diphosphonate**, did not influence DXR and this may indicate that nonphagocytic circulating monocytes may be more important in DXR. However, adoptive transfer of splenocytes from a **macrophage** depleted, xenoactivated donor did not accelerate xenograft rejection, while splenocytes from a nondepleted xenoactivated donor did, thereby supporting the importance of monocytes and macrophages in this phase of xenograft rejection.

11/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

13225067 BIOSIS Number: 99225067
Influence of **macrophage** depletion on bacterial translocation and rejection in small bowel **transplantation**
Fryer J; Grant D; Jiang J; Metrakos P; Ozcay N; Ford C; Garcia B; Behme R ; Zhong R
303 East Superior St., Suite 528, Chicago, IL 60611, USA
Transplantation (Baltimore) 62 (5). 1996. 553-559.
Full Journal Title: Transplantation (Baltimore)
ISSN: 0041-1337
Language: ENGLISH
Print Number: Biological Abstracts Vol. 102 Iss. 010 Ref. 140697
Rejection and sepsis can be intimately related following small bowel **transplantation** when rejection compromises normal intestinal barrier mechanisms and bacterial translocation results. Macrophages play a role in controlling the egress of intestinal luminal bacteria sbd and they have

also been implicated in allograft rejection. In this study, the role of macrophages in rejection and bacterial translocation was evaluated by depleting macrophages in donors and/or recipients of rat small bowel allografts with injection of liposome-encapsulated **dichloromethylene diphosphonate** (CL-2MDP). In preliminary studies, we demonstrated that a single intraperitoneal injection of liposome-encapsulated CL-2MDP (350 mg/kg) depleted ED2-positive macrophages by gt 90% in the liver mesenteric lymph nodes and proximal and distal small bowel, and by approximately 50% in the spleen. ED1-positive macrophages were depleted by gt 90% in the liver and by approximately 50% at the other sites. ED3-positive macrophages were completely depleted. Dendritic cells were gt 90% depleted in the spleen and mesenteric lymph nodes, but were not depleted in the small bowel. **Macrophage** depletion in the donor resulted in increased translocation of bacteria to the peritoneal cavity (P=0.03) if recipient macrophages were present. With histopathologic analysis, a significantly milder rejection with less arteritis was seen in the allografts of the recipient **macrophage** -depleted group compared with nondepleted controls (P=0.045). This suggests that recipient macrophages play an important role in rejection. With **macrophage** depletion in both the donor and the recipient, **graft** survival was prolonged significantly (13.2 +- 1.9 days) compared with non-**macrophage**-depleted controls (9.2 +- 1.3 days) (P=0.003). These studies suggest that strategies targeting recipient macrophages may be useful in controlling small bowel allograft rejection without increasing bacterial translocation.

11/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

13103482 BIOSIS Number: 99103482
Failure to reject an allografted tumor after elimination of macrophages in mice
Ushio Y; Yamamoto N; Sanchez-Bueno A; Yoshida R
Dep. Cell Biol., Osaka Biosci. Inst., 6-2-4 Furuedai, Suita, Osaka 565, Japan
Microbiology and Immunology 40 (7). 1996. 489-498.
Full Journal Title: Microbiology and Immunology
ISSN: 0385-5600
Language: ENGLISH
Print Number: Biological Abstracts Vol. 102 Iss. 005 Ref. 068931
After an i.p. **transplantation** of an allogeneic tumor (Meth A) to C57BL/6 mice, a **macrophage** (M-PHI)-rich, non-T, non-NK cell population is induced as the major infiltrate and cytotoxic cells. We here evaluated the role of the M-PHI-s in the rejection of allografted Meth A cells and characterized the M-PHI-s in comparison with other well-known M-PHI-s. At all time intervals after **transplantation**, the highest cytotoxic activities against Meth A tumor were obtained with the M-PHI-rich population. In addition, the lymphocyte-rich population had a significant but low cytotoxic activity, whereas two other population types, granulocytes and large granular cells, were inactive. When the M-PHI-rich or the T cell-depleted M-PHI-rich population was i.p. **transplanted** simultaneously with Meth A cells into untreated C57BL/6 mice, the tumor cells were rejected without growth. After specific elimination of M-PHI-s by in vivo application of **dichloromethylene diphosphonate** -containing liposomes, the cytotoxic activity against Meth A cells was hardly induced at the **transplantation** site of Meth A cells and the allografted Meth A tumor continued to grow, indicating that a type of M-PHI is the effector cell essential for the rejection. In contrast to other well-known M-PHI-s, the cytotoxic activity against Meth A cells was

cell-to-cell contact dependent and soluble factor (e.g., NO and TNF-alpha) independent. Moreover, the cytotoxic activity of the M-PHI-s (H-2-b) against 51Cr-labeled Meth A (H-2-d) cells was inhibited by the addition of unlabeled H-2-d, but not H-2-a, H-2-k or H-2-b, lymphoblasts as well as Meth A cells, implying the specific interaction of the M-PHI-s with H-2-d cells.

11/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11760346 BIOSIS Number: 98360346
Circulation of Human Hematopoietic Cells in Severe Combined Immunodeficient Mice After Cl-2MDP-Liposome-Mediated **Macrophage** Depletion
Fraser C C; Chen B P; Webb S; Van Rooijen N; Kraal G
3155 Porter Dr., Paolo Alta, CA 94304, USA
Blood 86 (1). 1995. 183-192.
Full Journal Title: Blood
ISSN: 0006-4971
Language: ENGLISH
Print Number: Biological Abstracts Vol. 100 Iss. 004 Ref. 052184
Intravenous injection of **dichloromethylene diphosphonate** (Cl-2MDP) encapsulated in liposomes results in specific elimination of macrophages in the spleen and liver of normal mice. Severe combined immunodeficient (SCID) mice were treated with Cl-2MDP-liposomes followed by injection of human peripheral blood leukocytes. Control SCID mice had no detectable human cells within 72 hours as determined by fluorescence-activated cell sorting (FACS) analysis. However, Cl-2MDP-liposome-treated animals maintained a large proportion (%) of human cells in peripheral blood and spleen for at least 12 days. C-2MDP-liposome-injected SCID mice that had previously been **implanted** with human fetal thymus and liver showed a transient increase in human cell content in peripheral blood, and an accumulation of human cells specific to the white pulp of the spleen. These results indicate that murine mononuclear phagocytic cells may play an important role in the clearance of human cells injected intravenously or generated endogenously in SCID mice and that Cl-2MDP-liposome-mediated **macrophage** depletion allows human hematopoietic cells to circulate and survive in SCID mice, thereby expanding the potential for studying human cellular processes in vivo.

11/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11270191 BIOSIS Number: 97470191
Prevention of corneal allograft rejection in rats treated with subconjunctival injections of liposomes containing **dichloromethylene diphosphonate**
Van Der Veen G; Broersma L; Dijkstra C D; Van Rooijen N; Van Rij G; Van Der Gaag R
Neth. Ophthalmic Res. Inst., Dep. Ophthalmo-Immunol., P.O. Box 12141, 1100 AC Amsterdam, NET
Investigative Ophthalmology & Visual Science 35 (9). 1994. 3505-3515.
Full Journal Title: Investigative Ophthalmology & Visual Science
ISSN: 0146-0404
Language: ENGLISH
Print Number: Biological Abstracts Vol. 098 Iss. 009 Ref. 124503

Purpose: The drug **dichloromethylene diphosphonate** (CL2MDP) encapsulated in liposomes depletes macrophages but not other immunocompetent cells. The authors investigated whether subconjunctival injection of CL2MDP containing liposomes (CL2MDP-LIP) could prolong survival of corneal allografts in rats. Methods: Male Fisher rats received orthotopic corneal **grafts** of Dark Agouti origin. Rats were treated postoperatively with subconjunctival injections of 0.1 ml CL2MDP-LIP at the time of **transplantation** and on days 2, 4, 6, and 8 after **transplantation** . Control groups received either liposomes containing phosphate-buffered saline subconjunctivally at the same time points or no additional treatment. Corneal **grafts** were evaluated every other day and were scored for neovascularization, opacity, and edema. Immunohistologic evaluation was performed 12 and 19 days after surgery. Results: Corneal **grafts** in both control groups were rejected within 17 days. In the C12MDP-LIP treated rats, **grafts** were not rejected during the maximum follow-up of 100 days. Cellular infiltration in these **grafts** was clearly reduced. There was also a strong reduction in neovascularization of the cornea. Conclusions: Rejection of orthotopic allogeneic corneal **grafts** could be prevented by repeated subconjunctival injection of C12MDP-LIP.

11/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

10074560 BIOSIS Number: 95074560
THE ROLE OF NATURAL ANTIBODIES AND ABO H BLOOD GROUPS IN **TRANSPLANTATION** OF HUMAN LYMPHOID CELLS INTO MICE
HUPPES W; PAULONIS J; DIJK H; VAN ROOIJEN N; VAN BERKKUM D W
C/O INST. APPLIED RADIOBIOLOGY IMMUNOLOGY TNO, P.O. BOX 5815, NL-2280 HV RIJSWIJK, THE NETHERLANDS.
EUR J IMMUNOL 23 (1). 1993. 26-32. CODEN: EJIMA
Full Journal Title: European Journal of Immunology
Language: ENGLISH
Recently, evidence was presented that natural antibodies (NAb) are a crucial barrier to human cellular engraftment in severely immunosuppressed normal mice (Eur. J. Immunol. 1992. 22: 197.). In this report we show that normal mouse serum contains low titers of NAb against human cells of blood groups type O (H) and B and high titers against human cells of blood group A. Accordingly, human peripheral blood leukocytes (PBL) of group O (H) and B donors could be **grafted** successfully into normal BCBA mice (H-2b/k) following irradiation with high dose total body irradiation (TBI). PBL of blood group type A donors did not engraft in normal mice but could be **transplanted** without difficulty in B cell-deficient CBA/N mice which lack NAb, after conditioning with high dose TBI. Treatment of lethally irradiated normal BCBA mice with cobra venom factor (COF), which eliminates the third factor of complement, and liposomes containing **dichloromethylene diphosphonate** (Cl2DMP), which eliminates macrophages, resulted in engraftment of human blood group type A PBL. This implies that the NAb barrier for discordant xenogeneic cell **transplantation** can be abrogated. A method utilizing directly labeled probes and flow cytometry is described for the quantitation in mouse serum of NAb, reacting with human cells. Using sera of H-2b/k mice we show that murine NAb react with human stem cells, granulocytes, lymphocytes and monocytes of blood group A and only weakly with similiar cells from blood group O (H) and B donors. Sera of H-2b, H-2d and H-2k mice of different ages and microflora possess NAb against human erythrocytes of blood group type A and occasionally demonstrate weak titers against erythrocytes of blood groups B and O (H) and the Rhesus factor.

11/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

9056263 BIOSIS Number: 93041263
IS EARLY REPOPULATION OF **MACROPHAGE**-DEPLETED LYMPH NODE INDEPENDENT OF BLOOD MONOCYTE IMMIGRATION?
MEBIUS R E; MARTENS G; BREVE J; DELEMARRE F G A; KRAAL G
DEP. CELL BIOL., VRIJE UNIV., VAN DER BOECHORSTSTRAAT 7, 1085 BT AMSTERDAM, NETHERLANDS.
EUR J IMMUNOL 21 (12). 1991. 3041-3044. CODEN: EJIMA
Full Journal Title: European Journal of Immunology
Language: ENGLISH
Popliteal lymph nodes (LN) of mice were depleted of their **macrophage** (M.PHI.) populations in the subcapsular sinus and medulla by subcutaneous injection of **dichloromethylene diphosphonate** (Cl2MDP)-containing liposomes into the footpads. Complete restoration of both M.PHI. populations could be observed as late as 5 months after liposome administration. This relatively long repopulation time could be due to a depot of liposomes, directly killing all M.PHI. precursors after extravasation into the interstitial tissue of the footpad. On the other hand, local interstitial precursors with very low turnover rates may have been depleted in the interstitial tissue of the hind leg. Therefore, two different types of experiments were performed; one in which M.PHI.-depleted LN were replaced by control LN at various time points after liposome treatment, and another whereby M.PHI.-depleted LN were **transplanted** into control animals. When liposome-treated, M.PHI.-depleted LN were **transplanted** into control animals, a complete restoration of both populations in the subcapsular sinus and medulla could be observed within 5 weeks. Control LN **transplanted** into a Cl2MDP-liposome-treated leg showed a rapid disappearance of M.PHI. from the subcapsular sinus and medulla and these cell populations remained absent for at least 7-8 weeks after liposome treatment, when the first cells started to reappear. Complete repopulation of these area by M.PHI. took as long as 15 weeks. Using labeled liposomes the presence of a continuous liposome depot was found to be very unlikely. These results suggest that the population of precursor cells that will give rise to M.PHI. in the subcapsular sinus and medulla of a LN is probably contained within the interstitial tissue and is almost independent of precursor supply from the blood compartment.

11/7/9 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

13097501 PASCAL No.: 97-0394489
Facilitated engraftment of human hematopoietic cells in severe combined immunodeficient mice following a single injection of Cl SUB 2 MDP liposomes
TERPSTRA W; LEENEN P J M; VAN DEN BOS C; PRINS A; LOENEN W A M; VERSTEGEN M M A; VAN WYNGAARDT S; VAN ROOIJEN N; WOGNUM A W; WAGEMAKER G; WIELENGA J J; LOEWENBERG B
Institute of Hematology, Erasmus University, Rotterdam, Netherlands; Department of Immunology, Erasmus University, Rotterdam, Netherlands; Wilhelmina Children's Hospital, Utrecht, Netherlands; Department of Biochemistry, University of Pretoria, South Africa; Department of Cell Biology and Immunology, Medical Faculty, Free University, Amsterdam, Netherlands
Journal: Leukemia, 1997, 11 (7) 1049-1054

ISSN: 0887-6924 CODEN: LEUKED Availability: INIST-21129; 354000067444530220
No. of Refs.: 50 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: United Kingdom
Language: English

Transplantation of normal and malignant human hematopoietic cells into severe combined immunodeficient (SCID) mice allows for evaluation of long-term growth abilities of these cells and provides a preclinical model for therapeutic interventions. However, large numbers of cells are required for successful engraftment in preirradiated mice due to residual **graft** resistance, that may be mediated by cells from the mononuclear phagocytic system. Intravenous (i.v.) injection of liposomes containing **dichloromethylene diphosphonate** (CI SUB 2 MDP) may eliminate mouse macrophages in spleen and liver. In this study outgrowth of acute myeloid leukemia (AML) cells and umbilical cord blood (UCB) cells in SCID mice conditioned with a single i.v. injection of CI SUB 2 MDP liposomes In addition to sublethal total body irradiation (TBI) was compared to outgrowth of these cells in SCID mice that had received TBI alone. A two- to 10-fold increase in outgrowth of AML cells was observed in four cases of AML. Administration of 10 SUP 7 UCB cells reproducibly engrafted SCID mice that had been conditioned with Cl SUB 2 MDP liposomes and TBI, whereas human cells were not detected in mice conditioned with TBI alone. As few as 2 x 104 purified CD34 SUP + UCB cells engrafted in all mice treated with Cl SUB 2 MDP liposomes. In SCID mice treated with **macrophage** depletion unexpected **graft** failures were not observed. Histological examination of the spleen showed that TBI and CI SUB 2 MDP liposomes i.v. resulted in a transient elimination of all **macrophage** subsets In the spleen, whereas TBI had a minor effect. CI SUB 2 MDP liposomes were easy to use and their application was not associated with appreciable side-effects. CI SUB 2 MDP liposome pretreatment in combination with TBI allows for reproducible outgrowth of high numbers of human hematopoietic cells in SCID mice.

11/7/10 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

12208947 PASCAL No.: 95-0426561
Circulation of human hematopoietic cells in severe combined immunodeficient mice after Cl SUB 2 MDP-liposome-mediated **macrophage** depletion
FRASER C C; CHEN B P; WEBB S; VAN ROOIJEN N; KRAAL G
Free univ., medical fac., dep. histology, Amsterdam, Netherlands
Journal: Blood, 1995, 86 (1) 183-192
ISSN: 0006-4971 Availability: INIST-3178; 354000051603390230
No. of Refs.: 38 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: English

Intravenous injection of **dichloromethylene diphosphonate** (CI SUB 2 MDP) encapsulated in liposomes results in specific elimination of macrophages in the spleen and liver of normal mice. Severe combined immunodeficient (SCID) mice were treated with CI SUB 2 MDP.liposomes followed by injection of human peripheral blood leukocytes. Control SCID mice had no detectable human cells within 72 hours as determined by fluorescence-activated cell sorting (FACS) analysis. However, CI SUB 2 MDP-liposome-treated animals maintained a large proportion (%) of human

cells in peripheral blood and spleen for at least 12 days. CI SUB 2 MDP-liposome-injected SCID mice that had previously been **implanted** with human fetal thymus and liver showed a transient increase in human cell content in peripheral blood, and an accumulation of human cells specific to the white pulp of the spleen. These results indicate that murine mononuclear phagocytic cells may play an important role in the clearance of human cells injected intravenously or generated endogenously in SCID mice and that CI SUB 2 MDP-liposome-mediated **macrophage** depletion allows human hematopoietic cells to circulate and survive in SCID mice, thereby expanding the potential for studying human cellular processes in vivo. (c) 1995 by The American Society of Hematology.

11/7/11 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08297965 95317538
Role of Kupffer cells in cold ischemia/reperfusion injury of rat liver.
Imamura H; Sutto F; Brault A; Huet PM
Andre-Viallet Clinical Research Center, Hopital Saint-Luc, Montreal, Quebec, Canada.
Gastroenterology (UNITED STATES) Jul 1995, 109 (1) p189-97, ISSN 0016-5085 Journal Code: FH3
Languages: ENGLISH
Document type: JOURNAL ARTICLE
BACKGROUND & AIMS: Kupffer cell activation is hypothesized to play an etiopathogenic role in storage-related **graft** failure after liver **transplantation** . The aim of this study was to verify whether the elimination of Kupffer cells modifies the magnitude of cold ischemia/reperfusion injury of the liver. METHODS: Rat Kupffer cells were eliminated by an intravenous injection of liposome-encapsulated **dichloromethylene diphosphonate** . Livers from control and treated rats were isolated and perfused before and after 24-hour cold ischemia in the University of Wisconsin solution (4 degrees C). Hepatocyte and sinusoidal endothelial cell functions were evaluated by taurocholate and hyaluronic acid elimination, respectively. Liver **transplantation** was also performed using control and treated donor livers stored under identical conditions. RESULTS: Compared with baseline values, similar alterations were found in both groups after cold ischemia for hepatocyte function (intrahepatic resistance, bile secretion, lactate dehydrogenase release, oxygen consumption, and taurocholate intrinsic clearance) and for sinusoidal endothelial cell function (hyaluronic acid intrinsic clearance). The 10-day survival rate of animals undergoing **transplantation** was not different between the groups (6 of 15 vs. 4 of 15, control vs. treated donor livers, respectively). CONCLUSIONS: The presence or absence of Kupffer cells does not modify the effect of 24-hour cold ischemia/reperfusion on the rat liver.

11/7/12 (Item 1 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci

15668540 Genuine Article#: WY032 Number of References: 65
Title: Transient suppression of **macrophage** functions by liposome-encapsulated drugs
Author(s): vanRooijen N (REPRINT) ; Bakker J; Sanders A
Corporate Source: VRIJE UNIV AMSTERDAM,DEPT CELL BIOL & IMMUNOL, FAC MED/NL-1081 BT AMSTERDAM//NETHERLANDS/ (REPRINT)

Journal: TRENDS IN BIOTECHNOLOGY, 1997, V15, N5 (MAY), P178-185
ISSN: 0167-7799 Publication date: 19970500
Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, OXON, ENGLAND OX5 1GB
Language: English Document Type: ARTICLE
Abstract: Macrophages play an important role in host defense reactions, for example, by phagocytosis of particulate materials. This process also results in the rapid removal of targeting devices such as liposomes and adenovirus vectors and of nonautologous **grafted** cells and materials. Another aspect of **macrophage** function is their production and secretion of proinflammatory cytokines. Transient and organ-specific suppression of **macrophage** function by liposome-mediated manipulation has been shown to improve the efficacy of drug and gene targeting and to reduce the symptoms of inflammatory reactions.

11/7/13 (Item 2 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci

15491029 Genuine Article#: WL183 Number of References: 35
Title: Chronic stimulation of the hypothalamus-pituitary-adrenal axis in rats by interleukin 1 beta: Central and peripheral mechanisms
Author(s): vanderMeer MJM; Sweep CGJ; Pesman GJ; Tilders FJH; Hermus ARMM (REPRINT)
Corporate Source: UNIV NIJMEGEN HOSP,DEPT MED, DIV ENDOCRINOL, POB 9101/NL-6500 HB NIJMEGEN//NETHERLANDS/ (REPRINT); UNIV NIJMEGEN HOSP,DEPT MED, DIV ENDOCRINOL/NL-6500 HB NIJMEGEN//NETHERLANDS/; UNIV NIJMEGEN HOSP,DEPT EXPT & CHEM ENDOCRINOL/NL-6500 HB NIJMEGEN//NETHERLANDS/; VRIJE UNIV AMSTERDAM,DEPT PHARMACOL, NEUROSCI RES INST/AMSTERDAM//NETHERLANDS/
Journal: CYTOKINE, 1996, V8, N12 (DEC), P910-919
ISSN: 1043-4666 Publication date: 19961200
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399
Language: English Document Type: ARTICLE
Abstract: The authors have studied mechanisms which could be involved in the sustained activation of the hyp othalamus-pituitary-adrenal (HPA) axis during continuous infusion of rats with recombinant human interleukin-1 beta (IL-1 beta). First, the effects of 3 days of intracerebroventricular (i.c.v.) infusion of rats with IL-1 on plasma adrenocorticotropin (ACTH) and corticosterone (B) levels were investigated, Thereafter, changes in plasma ACTH and B levels were followed in rats intraperitoneally (i.p.) infused with IL-1 beta after immunoneutralization of corticotropin-releasing hormone (CRH), hypophysectomy (HPX), **macrophage** depletion using **dichloromethylene diphosphonate** (Cl(2)MDP)-containing liposomes, adrenalectomy (ADX) and dexamethasone (DEX) administration, respectively, Infusion of IL-1 beta i.c.v., even in doses as low as 0.1 mu g/day, induced significant increases in plasma ACTH and B levels, HPX and ADX rats died within 18 h after starting the IL-1 beta infusion (0.5 mu g/day). Immunoneutralization of CRH significantly decreased and **macrophage** depletion significantly increased the stimulation of the HPA axis by IL-1 (4.0 mu g/day). Administration of high doses of DEX completely abolished the stimulation of the HPA axis by IL-1 beta (2.0 beta g/day). The present study demonstrates that lower doses of IL-1 beta were able to activate the HPA axis when infused i.c.v. compared with i.p. Regarding stimulation of the HPA axis by chronic i.p. infusion of IL-1 beta the present study: (1) provides evidence

that the CRH system is involved; (2) provides no evidence for a direct stimulatory effect of IL-1 beta on the release of B by the adrenal gland which is of suffcient magnitude to resist the stress of chronic i.p. IL-1 beta infusion; (3) shows that endogenous **macrophage** -derived mediators, induced by i.p. IL-1 beta infusion, express an overall inhibitory rather than a stimulatory effect on the activity of the HPA axis; (4) demonstrates that exogenous administration of DEX blocks the effect of IL-1 beta, which fits well in the concept of an immunoregulatory feedback between IL-1 beta and glucocorticoids.

11/7/14 (Item 3 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci

13617161 Genuine Article#: QB852 Number of References: 25
Title: RESPONSE OF ALVEOLAR **MACROPHAGE**-DEPLETED RATS TO HYPEROXIA
Author(s): BERG JT; WHITE JE; TSAN MF
Corporate Source: SAMUEL S STRATTON DEPT VET AFFAIRS MED CTR,RES SERV/ALBANY//NY/12208; SAMUEL S STRATTON DEPT VET AFFAIRS MED CTR,RES SERV/ALBANY//NY/12208; ALBANY MED COLL,DEPT PHYSIOL/ALBANY//NY/00000; ALBANY MED COLL,DEPT MED/ALBANY//NY/00000
Journal: EXPERIMENTAL LUNG RESEARCH, 1995, V21, N1 (JAN-FEB), P175-185
ISSN: 0190-2148
Language: ENGLISH Document Type: ARTICLE
Abstract: Recently an alveolar **macrophage** (AM)-depleted rat model has been characterized and it has been demonstrated that AM are required for the endotoxin-induced tumor necrosis factor (TNF) release into the alveolar space (I Appl Physiol 1993;74:2812-2819). The current study investigated the response of AM-depleted rats to hyperoxia and evaluated the potential role of AM in the pathogenesis of pulmonary O-2 toxicity. Rats were insufflated with Hanks' balanced salt solution (HBSS), liposome-encapsulated phosphate-buffered saline (PBS-liposomes), or liposome-encapsulated **dichloromethylene diphosphonate** (Cl(2)MDP-liposomes) and 2 days later exposed to 100% O-2. The effect of hyperoxia was assessed by parameters of O-2-induced lung injury (e.g., hematocrit value, pleural effusion volume, effusion protein to plasma protein ratio, and alveolar lavage fluid protein content), TNF release into the alveolar space, and survival. Insufflation of Cl(2)MDP-liposomes, but not HBSS or PBS-liposomes, caused a sustained depletion of >70% AM, which was associated with a slight but significant increase in the number of lavageable neutrophils. Twenty percent of AM-depleted rats survived longer than 74 h of O-2 exposure, while all rats insufflated with HBSS or PBS-liposomes died within 74 h ($p < .05$). No significant differences were detected in alveolar TNF release or in the extent of O-2-induced lung injury.
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